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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/772,445	01/29/2001	Hynda K. Kleinman	2600-109	1045

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EXAMINER

CHISM, BILLY D

ART UNIT

PAPER NUMBER

1654

DATE MAILED: 08/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/772,445

Applicant(s)

KLEINMAN ET AL.

Examiner

B. Dell Chism

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 08 June 2005.  
2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.  
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-40, 47-49, 53-61 and 133-175 is/are pending in the application.  
4a) Of the above claim(s) 9-10, 12, 20, 21, 37, 41-52, 62-132, 145, 154, 163 and 172 is/are withdrawn from consideration.  
5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.  
6) ☒ Claim(s) 1-8, 11, 13-19, 22-36, 38-40, 53-61, 133-144, 146-153, 155-162, 164-171 and 173-175 is/are rejected.  
7) ☒ Claim(s) 1, 2, 5-8, 11, 13, 23, 24, 33-36, 137 and 164 is/are objected to.  
8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.  
10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)  
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)  
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.  
4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.  
5) ☐ Notice of Informal Patent Application (PTO-152)  
6) ☐ Other: \_\_\_\_\_.

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### **DETAILED ACTION**

1. Applicant's election without traverse of Group I, and species thymosin beta 4, in the reply filed on 08 June 2005 is acknowledged. Claims 1-8, 11, 13-19, 22-36, 38-40, 53-61, 133-144, 146-153, 155-162, 164-171, and 173-175 are under consideration. Claims 12, 20-21, 37, 41-52, 62-132, 145, 154, 163 and 172 are withdrawn from consideration as being drawn to non-elected subject matter.

#### ***Claim Objections***

2. Claims 1, 2, 5-8, 11, 13, 23-24, 33-36, 137 and 164 are objected to because of the following informalities: claim 1, line 1, uses the phrase "would healing" wherein the phrase should read "wound-healing", and claims 1, 2, 5-8, 11, 13, 23-24, and 33-36 are objected to for reciting "wound healing" wherein Applicants should state "wound-healing" with a hyphen, as initially used in claim 1; Claim 2 is objected to for the term "an isoforms" wherein the claim should read "an isoform" or "isoforms"; claims 1, 23, 137 and 164 are objected to for not being in sequence compliance for lacking a sequence identifier before OR after the recitation of the amino acid sequence LKKTET. Appropriate correction is required.

#### ***Claim Rejections - 35 USC § 103***

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claims 1-2, 5-8, 11, 13, 16-19, 22-28, 33-36, 38-40, 53-61, 133-138, 141-144, 146-147, 150-153, 155-156, 159-162, 164-165, 168-171, and 173-175 rejected under 35 U.S.C. 103(a) as

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being unpatentable over Malinda et al. 1997 (FASEB Journal, Vol. 11, No. 6, pages 474-481) in combination with Stevenson et al. (US 6,602,519 B1).

Malinda et al. teaches the wound-healing activity of thymosin.beta.4 on endothelial cells (see abstract). However, Malinda et al. does not teach in vivo uses or formulations as instantly claimed.

Stevenson et al. teaches wound-healing using oxidized thymosin.beta.4 (TB4). Stevenson et al. also teach multiple formulations for multiple deliveries for multiple (column 5, lines 34-67 and column 6, lines 1-67). Additionally, Figure 8 a-d teaches wound-healing and claims 1,2 and 4 teach the treatment of inflammatory conditions, i.e., connective tissues, vascular, intestinal, blood and skin and transplantation/prosthetic sites against infection, with TB4 compositions. Stevenson et al. also teaches physiologically active variants.

It would have been obvious to one of ordinary skill in the art at the time of filing of the application to use TB4 in wound-healing as taught above, and to apply TB4 in varying formulations to skin, in vivo, topically, to connective tissues and intestinal tissue, for example, and to be done so with reasonable expectation of success.

***Claim Rejections - 35 USC § 112***

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 137-144, 146-153, 155-162 and 164-171 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for promoting wound-healing, does not reasonably provide enablement for regeneration of all tissues or extremities, or preventing or

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reducing scar tissue from forming in a wound. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same..." The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring ingenuity beyond that to be expected of one of ordinary skill in the art (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Additionally, the courts have determined that "where a statement is, on its face, contrary to generally accepted scientific principles, a rejection for failure to teach how to make and/or use is proper" (In re Marzocchi, 169 USPQ 367 (CCPA 1971)). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977) and have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986). Among the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation

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needed. The instant disclosure fails to meet the enablement requirement for the following reasons:

*The nature of the invention:* The claimed invention is drawn to a method for promoting wound-healing by administration of thymosin.beta.4 to the wound.

*The state of the prior art and the predictability or lack thereof in the art:* The art teaches that the TB4 significantly accelerates the rate of migration into wounded area (Malinda et al. 1997, FASEB Journal, Vol. 11, No. 6, pages 474-481). The art also teaches that TB10, an isoform of TB4, stimulates cell wound healing activity (Sun et al. 1996, J. Biol. Chem., Vol. 271, No. 16, pages 9223-9230). However, the art does not teach regeneration of all tissues, i.e., limb buds, or prevention or reduction of scar tissue in a wound. Therefore there is a lack of predictability regarding whether the claimed methods can regenerate all tissues or prevent and reduce scar tissue formation in a wound in entirety.

*The amount of direction or guidance present and the presence or absence of working examples:* Given the lack of predictability regarding regeneration, and prevention and reduction of scar tissue in the art, detailed teachings are required to be present in the disclosure to enable the skilled artisan to use the methods for complete regenerate any and all tissues, or prevention and reduction of scar tissue in a wound. Such teachings are absent. The specification only gives examples to treating dermal wounds and corneal tissue. There are no disclosures of how to use the methods as claimed for complete prevention and reduction of scar tissue in a wound or regeneration of any and all tissues.

*The breadth of the claims and the quantity of experimentation needed:* Given the lack of predictability found in the art regarding the regeneration of any and all tissues, and prevention or

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reduction of scar tissue formation in a wound and in the absence of sufficient disclosure in applicant's specification to overcome the lack of predictability in the art, it would require undue experimentation by one of skill in the art to be able to use the invention commensurate in scope with the claims.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 23 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 23 is indefinite wherein it is unclear as to whether the composition comprises both the LKKTET comprising sequence and also the conservative variants, or if the composition comprises one or the other.

Claims are rejected for depending from indefinite claims.

Claims 24-36 and 38-39 are rejected for depending from indefinite claims.

Claim 40 is rejected for the indefinite recitation of the phrase "eye tissue" wherein it is unclear as to whether all eye tissue is meant to be treated or just the corneal tissue as is given in the examples of the specification.

Claims 137-138, 141-144, 147, 150-153, 156 and 159-162 are rejected for the indefinite recitation of the term regeneration wherein it is unclear as to what are the metes and bounds of tissue regeneration, especially where the term "regeneration" could entail limb regeneration. Claim language should be narrowed to establish metes and bounds of regeneration.

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Claim 137 is rejected for the indefinite recitation of the term "replacing" wherein it is unclear as to whether the method requires removing old tissue and taking tissue from another source to replace the old tissue. If this is merely the repairing of wounds without transplantation then the term "replacing" should be dropped from the claim.

Claims 139-140, 146, 148-149, 155 and 157-158 are rejected for depending from an indefinite claim 37.

Claim 164 is rejected wherein it is unclear if a wound is being treated or if a healed wound is treated. The phrase "revitalizing scar tissue" is indicative of a healed wound as evidenced by the scar remaining. Thus, scar tissue revitalization is not a method of healing a wound. However, reducing scar tissue from forming is indicative of treatment during the healing process and therefore is definite.

Claims 165-171 are rejected for depending from indefinite claims.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to B. Dell Chism, whose telephone number is (571) 272-0962. The examiner can normally be reached on M-F 08:30 AM - 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, PhD can be reached on (571) 272-0974.

The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status



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information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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BDC

  
B. DELL CHISM  
PATENT EXAMINER